Amendments to the Claims

The listing of claims below is intended to replace all prior listings of the claims:

1. (Currently Amended) A method of inducing tolerance to an antigen in a patient, the method comprising:

administering to ~~the~~ a patient an agent which raises the effective cAMP concentration in a monocyte cell and granulocyte-macrophage colony stimulating factor (GMCSF) or a derivative thereof that has at least 50% of the ability of full length GMCSF to stimulate the production of granulocytes and macrophages from their progenitor cells and which in the presence of prostaglandin E causes monocytes to express IL-10,

whereby said administering induces tolerance to an antigen in the patient and thereby treats or prevents an aberrant or undesired immune or inflammatory response to the antigen.

2. (Original) A method according to Claim 1 wherein the agent which raises the effective cAMP concentration in a monocyte cell is any one or more of a prostaglandin or agonist thereof, a ß-adrenergic agent, a blocker of cAMP export from the cell, forskolin or a derivative thereof, a cAMP phosphodiesterase inhibitor, a cAMP analogue, or cholera toxin or a derivative or fragment thereof.

3. (Withdrawn) A method according to Claim 2 wherein the blocker of cAMP export from the cell is probenicid or progesterone.

4. (Withdrawn) A method according to Claim 2 wherein the cAMP analogue is Sp-adenosine 3',5'-cyclic monophosphorothioate or 8-bromoadenosine 3',5' cyclic monophosphate or dibutryryl cAMP.

5. (Original) A method according to Claim 2 wherein the prostaglandin or agonist thereof stimulates cAMP production in a monocyte.

6. (Previously Presented) A method according to Claim 2 wherein the prostaglandin or agonist thereof is any one of a prostaglandin E or an analogue thereof, prostaglandin E_2 or an analogue thereof, dinoprostone, gemeprost, misoprostol, alprostadil, limaprost, butaprost, 11-deoxy PGE1, AH23848, AH13205, or a 19-hydroxy PGE.

7. (Currently Amended) A method according to Claim 1 wherein the GMCSF is human GMCSF having the amino acid sequence of SEQ ID NO:2~~, or naturally occurring variants thereof~~.

8. (Previously Presented) A method according to Claim 1 wherein the GMCSF is sargramostim.

9. (Currently Amended) A method according to Claim 1 further comprising administering to the patient one or more of a monocyte chemotactic agent, a phosphodiesterase (PDE) inhibitor, and the antigen or a ~~derivative thereof~~ a portion of the antigen which can be presented by a class I or class II MHC molecule and which induces tolerance to the antigen.

10. (Original) A method according to Claim 9 wherein the monocyte chemotactic agent is MCP-1 or MIP-1α.

11. (Canceled)

12. (Previously Presented) A method according to Claim 9 wherein the PDE inhibitor is any one of 3-isobutyl-1-methylxanthine (IBMX), pentoxifylline (3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)-1H-purine-2,6-dione), rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), theophylline, or denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine).

13. (Previously Presented) A method according to Claim 9 wherein the PDE inhibitor is selective for type IV PDE.

14. (Original) A method according to Claim 13 wherein the PDE inhibitor selective for type IV PDE is any one of rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine), or CDP840, RP73401 or RS33793.

15. (Canceled)

16. (Currently Amended) A method according to Claim 9 wherein one or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or ~~derivative~~ portion thereof is administered (i) locally at a site where tolerance is required, (ii) systemically, (iii) orally, or (iv) as a suppository or capsule.

17-19. (Canceled)

20. (Withdrawn) A method according to Claim 16 wherein the suppository or capsule has an enteric coating for release of the one or more of the agent which raises the

effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or derivative thereof in the bowel of the patient.

21. (Withdrawn) A method according to Claim 16 wherein at least the GMCSF or derivative thereof is administered subcutaneously or intravenously.

22. (Currently Amended) A method according to Claim 9 wherein any two or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or ~~derivative~~ portion thereof are administered simultaneously.

23. (Currently Amended) A method of combating ~~a disease or condition associated with transplant rejection~~ graft versus host disease or host versus graft disease comprising:

performing the method according to Claim 1, wherein said administering is effective to combat ~~a disease or condition associated with transplant rejection~~ graft versus host disease or host versus graft disease.

24. (Canceled)

25. (Currently Amended) A method according to Claim 23 wherein one or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof that has at least 50% of the ability of full length GMCSF to stimulate the production of granulocytes and macrophages from their progenitor cells and which in the presence of prostaglandin E causes monocytes to express IL-10, a monocyte chemotactic agent, a PDE inhibitor, and the antigen or ~~derivative~~ portion thereof is administered prior to the transplant.

26. (Previously Presented) A method according to Claim 23 wherein the antigen is HLA-A2.

27. (Withdrawn) A method of treating an autoimmune disease or condition comprising:

performing the method according to Claim 1, wherein said administering is effective to treat an autoimmune disease or condition.

28. (Withdrawn) A method according to Claim 27 wherein the autoimmune disease is selected from the group consisting of primary myxoedema, thyrotoxicosis, pernicious

anaemia, autoimmune atrophic gastris, Addison's disease, insulin-dependent diabetes mellitus (IDDM), Goodpasture's syndrome, myasthenia gravis, sympathetic ophthalmia, multiple sclerosis (MS), autoimmune haemolytic anaemia, idiopathic leucopenia, ulcerative colitis, dermatomyositis, scleroderma, mixed connective tissue disease, rheumatoid arthritis, irritable bowel syndrome, systemic lupus erythromatosus (SLE), Hashimoto's disease, thyroiditis, Behcet's disease, coeliac disease/dermatitis herpetiformis, renal vasculitis, and demyelinating disease.

29. (Withdrawn) A method according to Claim 27 wherein the antigen is a self-antigen.

30. (Withdrawn) A method according to Claim 27, wherein the autoimmune disease is pernicious anaemia, and the antigen is vitamin B_{12}; the disease is Addison's disease, and the antigen is adrenal antigen; the disease is IDDM, and the antigen is glutamic acid decarboxylase (GAD), insulin, or IA-2; the disease is Goodpasture's syndrome or renal vasculitis, and the antigen is renal antigen or endothelial antigen; the disease is myasthenia gravis, and the antigen is the acetyl choline receptor; the disease is sympathetic ophthalmia, and the antigen is ocular antigen; the disease is multiple sclerosis (MS), and the antigen is myelin basic protein (MBP), proteolipid protein (PLP), or myelin oligodendrocyte glycoprotein (MOG); the disease is autoimmune haemolytic anaemia, and the antigen is red cell antigen; the disease is idiopathic leucopenia, and the antigen is leukocyte antigen; the disease is ulcerative colitis, and the antigen is a food antigen or a viral antigen; the disease is dermatomyositis, and the antigen is smooth muscle antigen; the disease is scleroderma, and the antigen is a connective tissue antigen; the disease is mixed connective tissue disease, and the antigen is a connective tissue antigen; the disease is irritable bowel syndrome, and the antigen is a food antigen; the disease is systemic lupus erythmatosus (SLE), and the antigen is a histone protein or immunoglobulin heavy chain; ~~if~~ the disease is Hashimoto's disease, primary myxoedema or thyrotoxicosis, and the antigen is thyroid antigen; the disease is rheumatoid arthritis, and the antigen is type II collagen or a heat shock protein (HSP); the disease is thyroiditis, and the antigen is thyroglobulin; the disease is Behcet's disease, and the antigen is Sag, HLA-B44, B51, or HSP65; the disease is Coeliac disease/Dermatitis herpetiformis, and the antigen is gliadin or the α fraction thereof; or the disease is demyelinating disease, and the antigen is myelin.

31. (Withdrawn) A method of treating an allergic disease or condition in a patient comprising:

performing the method according to Claim 1, wherein said administering is effective to treat an allergic disease or condition in the patient.

32. (Withdrawn) A method according to Claim 31 wherein the allergic disease or condition is allergic asthma.

33. (Withdrawn) A method according to Claim 31, wherein the antigen is a mite allergen, a dust allergen, a cat allergen, a dog allergen or a horse allergen.

34. (Withdrawn) A method according to Claim 1, wherein the induced tolerance to the antigen is effective to treat an aberrant or undesired immune or inflammatory response to the antigen in the patient.

35. (Withdrawn) A method according to Claim 34 wherein the aberrant or undesired immune or inflammatory response involves a deficiency in IL-10 production.

36. (Withdrawn) A composition comprising an agent which raises the effective cAMP concentration in a monocyte cell and granulocyte-macrophage colony stimulating factor (GMCSF) or a derivative thereof.

37. (Withdrawn) A composition according to Claim 36 wherein the agent which raises the effective cAMP concentration in a monocyte cell is any one or more of a prostaglandin or agonist thereof, a β-adrenergic agent, a blocker of cAMP export from the cell, forskolin or a derivative thereof, a cAMP phosphodiesterase inhibitor, a cAMP analogue, or cholera toxin or a derivative or fragment thereof.

38. (Withdrawn) A composition according to Claim 37 wherein the blocker of cAMP export from the cell is probenicid or progesterone.

39. (Withdrawn) A composition according to Claim 37 wherein the cAMP analogue is Sp-adenosine 3′,5′-cyclic monophosphorothioate or 8-bromoadenosine 3′,5′ cyclic monophosphate.

40. (Withdrawn) A composition according to Claim 37 wherein the prostaglandin or agonist thereof stimulates cAMP production in a monocyte.

41. (Withdrawn) A composition according to Claim 37 wherein the prostaglandin or agonist thereof is a prostaglandin E or an analogue thereof, prostaglandin E_2 or

an analogue thereof, dinoprostone, gemeprost, misoprostol, alprostadil, limaprost, butaprost, 11-deoxy PGE1, AH23848, AH13205, or a 19-hydroxy PGE.

42. (Withdrawn) A composition according to Claim 36 wherein the GMCSF is human GMCSF having the amino acid sequence of SEQ ID NO:2, or naturally occurring variants thereof.

43. (Withdrawn) A composition according to Claim 36 wherein the GMCSF is sargramostim.

44. (Withdrawn) A composition according to Claim 36 further comprising one or more of a monocyte chemotactic agent, a phosphodiesterase (PDE) inhibitor, and an antigen or derivative thereof.

45. (Withdrawn) A composition according to Claim 44 wherein the monocyte chemotactic agent is MCP-1 or MIP-1α.

46. (Canceled)

47. (Withdrawn) A composition according to Claim 44 wherein the PDE inhibitor is any one of 3-isobutyl-1-methylxanthine (IBMX), pentoxifylline (3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)-1H-purine-2,6-dione), rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), theophylline, or denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine).

48. (Withdrawn) A composition according to Claim 44 wherein the PDE inhibitor is selective for type IV PDE.

49. (Withdrawn) A composition according to Claim 48 wherein the PDE inhibitor selective for type IV PDE is any one of rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine), or CDP840, RP73401 or RS33793.

50. (Canceled)

51. (Withdrawn) A pharmaceutical composition comprising the composition according to Claim 36 and a pharmaceutically acceptable carrier, diluent or excipient.

52-65. (Canceled)

66. (Withdrawn) A therapeutic system for inducing tolerance to an antigen in a patient, the system comprising an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof.

67. (Withdrawn) A therapeutic system according to Claim 66 further comprising one or more of the antigen, a monocyte chemotactic agent, and a phosphodiesterase (PDE) inhibitor.

68. (Canceled)

69. (Withdrawn) A therapeutic system according to Claim 67 wherein one or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or derivative thereof is in a preparation for (i) administration locally at a site where tolerance is required, (ii) systemic administration, (iii) oral administration, or (iv) administration as a suppository or capsule.

70-72. (Canceled)

73. (Withdrawn) A method of stimulating or enhancing granulysin expression in cells of a macrophage/monocyte lineage comprising administering to the cells a therapeutic system according to claim 66.

74. (Withdrawn) A method of treating a viral infection in a patient comprising administering to the patient a therapeutic system according to claim 66.

75. (Withdrawn) A method according to Claim 74 wherein the viral infection is a herpes simplex virus infection or a human papilloma virus infection.

76-77. (Canceled)

78. (Withdrawn) A method of stimulating or enhancing IL-10 expression in, and secretion from, cells of a macrophage/monocyte lineage comprising administering to the cells a therapeutic system according to claim 66.

79. (Withdrawn) A method of treating a tumour in a patient comprising administering to the patient a therapeutic system according to claim 66.

80-81. (Canceled)